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(54) Planar electrode.

(57) A planar electrode which enables easy multi-point simultaneous stimulation and measurement of nerve cells as well as signal transmission and observation throughout many cells for more than a few days includes an insulating substrate, a multiplicity of equally spaced electrodes thereon, a wiring section in which lead wires are installed substantially radially from the electrodes, and an insulating layer covering the lead wires. The area of each electrode is in the range from 3×10^2 to 4×10^2 μm^2.

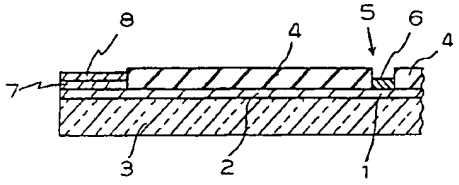

FIG.3

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This invention relates to a planar electrode which is used in the field of neurophysiology for electric measurement of biological activities, in particular, of the electric activities of nerve cells. This planar electrode comprises a large number of electrodes, and enables long-term culture of nerve cells on the electrodes, applies electric stimulation to nerve cells through electrodes during culture period, and is able to record electrical activities of nerve cells using the electrodes.

Recently, medical investigations on nerve cells and investigations of the possibility of using nerve cells as electronic elements have been actively pursued.

The interior of a nerve cell is separated from the exterior by the cell membrane, through which substances are delivered to and from the cell. The cell membrane exhibits different permeability to various substances. This property is called selective permeability.

The cell membrane of nerve cells exhibits selective permeability also to various types of ions. Moreover, this selectivity varies in accord with the cell condition. Inside the nerve cell in the resting state, the concentration of Na^+ is low and that of K^+ is high. Conversely, outside the cell, the concentration of Na^+ is high and that of K^+ is low. As a result, an ion concentration gradient is produced between the inside and the outside of the cell, and a potential difference (membrane potential) is developed. This membrane potential is negative inside the cell with respect to the outside of the cell and is generally around -70 mV for vertebrates. This membrane potential is called the resting membrane potential.

In the event that stimulation (generally electrical stimulation) is given to nerve cells and the membrane potential is changed from resting to positive (depolarization), if the magnitude of depolarization is below a certain threshold value, the selective permeability of the cell membrane to ions does not change and the action potential is not generated. When depolarization exceeds the threshold value, the selective permeability of the cell membrane to ions changes and the action potential is generated. As the action potential is generated, the ion concentration inside and outside the cell membrane varies. Measuring this potential change accompanied by the ion concentration change near the nerve cells (that is, the ion current) with electrodes enables the detection and investigation of nerve activities.

Conventionally, in order to measure the electrical activities of nerve cells, it is common practice to use a recording electrode and a stimulating electrode comprising glass, metal, or other electrodes, insert them in or between cells, and measure the electrical activities of nerve cells with the recording electrode when a stimulating current (or voltage) is applied from the stimulating electrode.

In addition to this, there are many modified methods such as the so-called whole cell patch clamp method, in which a cell is absorbed within a glass electrode formed into a dropping pipet with an about 1-μm-diameter tip end designed to break a part of the cell membrane, the inside of the cell body is refluxed with the liquid in the glass electrode, and electrical signals are emitted from this glass electrode to observe electric characteristics of the cell.

In the conventional technique and its modified methods, electrodes such as glass electrodes, which have to be larger than the cells themselves, must be used. As a result, primarily due to restrictions of space and operating accuracy, multi-point simultaneous measurements in which two or more recording electrodes are inserted simultaneously in one sample to record electrical activities of the nerve cells are extremely difficult.

In order to investigate the operation of the whole nerve circuit network, it is necessary to record many nerve cell activities simultaneously, and as the number of measuring points increases, the degree of difficulty increases, creating the problem that it is difficult to observe throughout a large number of cells.

In addition, because glass, metal, or other electrodes must be pierced into or between cells, there is another problem that the damage to the cell is serious and measurement over a long time such as extending for more than a few hours is difficult to carry out.

Because in the whole cell patch clamp method, the cell inside is refluxed with the liquid contained in the glass electrode, damage to the cell is even greater, restricting the measurerent time to about 1 hour.

Accordingly, a feature of the invention is to provide a planar electrode which solves these conventional problems and enables easy multi-point simultaneous stimulation and measurement of nerve cells as well as signal transmission and observation throughout many cells for more than just a few hours.

The invention features a planar electrode comprising an insulating substrate, a multiplicity of electrodes placed thereon with adjacent electrodes being equidistantly spaced, a wiring section in which lead wires are installed substantially radially from the electrodes, and an insulating layer covering the lead wires. The electrodes each have an area ranging from 3×10^2 to 4×10^2 μm^2.

It is preferable in the invention that the shortest electrode-to-electrode distance is from 10 to 1000 μm.

It is preferable in the invention that the insulating layers covering the lead wires have holes on each electrode and are provided nearly all over the surface of the insulating substrate except in the vicinity of the contacts of the lead wires with an external circuit.

It is preferable in the invention that the surface resistance of the electrode is 10 Ω/cm^2 or lower. For this reason, it is preferable to cover the surface of the electrode with either platinum, platinum black, or gold.

It is preferable in the invention that the center of a multiplicity of electrodes is located on each intersection of an 8 × 8 lattice.

It is desirable for the insulating substrate to be made of a transparent material, so that the nerve cell cultured on the insulating substrate can be easily observed. For similar reasons, it is desirable for the electrodes, the lead wires and the insulating layer to be made of a transparent material.

It is further preferable in the invention that the electrode and the lead wire each are made from indium tin oxide (ITO), tin oxide, Cr, Au, Cu, Ni, or Al.

In particular, the insulating layer is preferably made from either polyimide (PI) resin, negative photosensitive polyimide (NPI) resin, epoxy resin, acrylate resin, polyester resin, or polyamide resin.

The planar electrode of the invention enables detection of the transmission of signals between adjoining cell bodies in providing signals to nerve cells cultured on the planar electrode of the invention and measuring the signal between cells at the same time. This is because one cell body is arranged on the electrode, and it can be arranged with a high degree of probability that the cell body mediating the cell protrusions (e.g., dendrites and axons on nerve cells) will be located on adjoining electrodes by adjusting the shortest electrode-to-electrode distance to be nearly equal to the length of a nerve cell to be measured (that is, cell body, dendrites, axon) and equally spacing the electrodes.

Furthermore, arranging the lead wires extending from the electrodes substantially radially reduces the capacitive component (capacitance) between lead wires from the capacitance when they are arranged in parallel. The collapse of pulse signal waveform, electrical signals, is also reduced, and the time constant of the circuit becomes small, improving the response to quick pulse signals and therefore improving the follow-up to the component with fast nerve cell activities.

In addition, adjusting the electrode area in the range from 3 × 10^2 to 4 × 10^2 μm^2 enables application of electric stimulation to a cell over a long time exceeding few days as well as measurement of electric activities of the cell. In particular, in the lower end of the electrode area range, the planar electrode of the invention is suited for recording subtle cell activities, while in the higher end of the electrode area range, the invention is suited for applying electric stimulation to cells over a long time. Adjusting the electrode area to the above-mentioned range enables designing a planar electrode suited for a variety of applications.

In addition, in the planar electrode of the invention, bringing the shortest electrode-to-electrode distance to the desirable condition of 10-1000 μm results in a high possibility of locating the cell bodies on adjoining electrodes and connecting them via their axons, achieving an electrode-to-electrode distance convenient for investigating information transmission between nerve cells.

In the planar electrode of the invention, the desirable form of the insulating layer, in which the insulating layers covering lead wires have holes over each electrode and are installed on nearly the whole surface of the insulating substrate except the vicinity of the section where the lead wire comes in contact with the external circuit, allows easy formation of the required insulating layer by applying the insulating material comprising photo-sensitive resin to nearly the whole surface and removing the insulating layer on each electrode by a photo-etching method and opening holes to expose electrodes, thereby achieving easy production and minimizing the probability of insulation failure, which is very desirable.

Designing the electrodes and lead wires to be formed with transparent material enables easy observation of nerve cells cultured on the planar electrode, which is also very desirable.

Determining the surface resistance of the electrode section to achieve the desired range of 10 Ω/cm^2 or less substantially prevents polarization on the stimulating electrode surface of the nerve cell from occurring when a stimulating current is applied for a long time to nerve cells at a certain electrode and recording electrical activities (potential change) of the nerve cells corresponding to the stimulating current at other electrodes, thereby minimizing the effects (that is, artifacts) of stimulating current on potential recording waveform. In particular, because even after a stimulating current is applied over a long time, with the invention artifacts are small and the mode is free from change, so electrical activities of nerve cells before and after long stimulation can be compared.

In addition, when the electrode surface is covered with either platinum, platinum black, or gold to bring down the surface resistance of the electrode to 10 Ω/cm^2 or less, the platinum, platinum black, or gold comes into direct contact with nerve cells; because these metals are known to cause low cytotoxicity, they are suitable to achieve the objec-

tives of the invention.

Furthermore, in the planar electrode of the invention, locating the center of a multiplicity of electrodes at each intersection of 8 x 8 lattices secures the maximum number of electrodes which enables installation of lead wires substantially radially from the electrodes of the invention, which is very desirable.

This invention provides a planar electrode with excellent response capable of culturing nerve cells and achieving simultaneous multi-point measurement of electrical activities of nerve cells and long-term observation of signal transmission over many cells for more than several hours, which conventionally has been an impossible or very difficult result to achieve.

The required insulating layer pattern is easily formed by the photoetching method and provides a planar electrode which is easy to produce and has small probability of insulation failure. This method can readily produce an electrode in which the insulating layers on lead wires have holes over each electrode and are installed on nearly the whole surface of the insulating substrate except in the vicinity of the sections where the lead wires come in contact with the external circuit, as compared with a planar electrode in which an insulating layer is provided merely on the lead wires. This is achieved, for example, by applying an insulating material comprising photo-sensitive resin on nearly the whole surface and removing the insulating layer on each electrode to make a hole for exposing the electrode.

Because each electrode has small surface resistance and is coated with a substance of low cytotoxicity, when suitable electrodes are used to apply stimulating current and the potential change is recorded with other suitable electrodes, the invention provides a planar electrode with less polarization of electrodes and which provides stable recording even after stimulation is applied over a long time.

In addition, the preferred embodiment of the invention in which a multiplicity of electrodes each are located at intersecting points of 8 x 8 lattices provides a planar electrode with maximum number of electrodes which allows installation of lead wires nearly radially from the electrodes.

FIG. 1 is a plan view of an embodiment of the invention prior to the application of an insulating layer on the planar electrode of the invention showing electrodes and lead wires formed on an insulating substrate;

FIG. 2 is a partially notched view of the plan view of Fig. 1 having the insulating layer of an embodiment of the invention applied to a planar electrode;

FIG. 3 is a fragmentary cross sectional view of an embodiment of a planar electrode of the invention;

FIG. 4 shows a changing potential waveform recorded with other suitable electrodes before applying stimulating current over a long time using suitable electrodes in an embodiment of the planar electrode of the invention;

FIG. 5 shows the changing potential waveform recorded with other suitable electrodes after applying stimulating current over a long time using suitable electrodes in an embodiment of the planar electrode of the invention;

FIG. 6 shows the changing potential waveform recorded with other suitable electrodes before applying stimulating current over a long time with suitable electrodes, using a planar electrode which differs from the planar electrode of the invention only in that the electrode surface is not coated with gold;

FIG. 7 shows another kind of the changing potential waveform recorded with electrode after applying stimulating current over a long time with suitable electrodes, using a planar electrode which differs from the planar electrode of the invention only in that the electrode surface is coated with gold.

As the insulating substrate material used for the invention, a transparent substrate is desirable because microscopic observation is required after the cell culture as described above. Examples include glasses such as quartz glass, lead glass or borosilicate glass, or inorganic substances such as quartz, or organic substance with transparency such as polymethyl metacrylate or its copolymers, polystyrene, polyvinyl chloride, polyester, polypropylene, urea resin, and melamine resin. Considering mechanical strength in combination with transparency, though, inorganic substances are desirable.

As the electrode materials used for the invention, examples include indium tin oxide (ITO), tin oxide, Cr, Au, Cu, Ni and Al. In particular, the use of ITO or tin oxide produces a slightly yellowish transparent electrode which provides good visibility of nerve cells under the microscope and is advantageous in experimental operation, but ITO is particularly desirable for its good conductivity.

The same materials can be applied to lead wires, and ITO is again desirable for similar reasons to those mentioned for electrode materials.

It is not a particular restriction of the invention, but in general the thickness of the electrodes and lead wires should be about 50-500 nm and, in general, these materials are evaporated on the insulating substrate and formed in a desired pattern by etching using a photoresist.

As the insulating layer material used to insulate the lead wires used for the invention, examples include polyimide (PI) resin, epoxy resin, acrylate resin, polyester resin, polyamide resin, and other transparent resins.

These types of resin are applied on lead wires by conventional techniques to form an insulating layer. When the insulating material is a photosensitive resin which has photochemical polymerization properties, etc.,. it is desirable because patterns can be formed to provide holes on the insulating layer portion on the electrodes to expose the electrodes as described above.

In particular, when insulating material is PI and the cell to be cultured is a nerve cell, satisfactory growth takes place and therefore, it is very desirable. In addition, among types of PI, negative photosensitive polyimide (NPI) is most desirable because holes can be formed on the electrodes using a photo etching process after the negative photosensitive polyimide is applied over nearly the whole surface, in a manner similar to that in forming patterns of the wiring section.

The thickness of the insulating layer may be such that can impart insulating capability. This is not particularly limiting but in general, a thickness of 0.1-10 μm, specifically, one of 1-5 μm is desirable.

The planar electrode of the invention directly cultures cells and measures and records electrical activities of the cells. Depending on culture conditions or the type of cells, the size of cell body or the length of cell protrusion such as dendrites or axons may vary but 10-1000 μm is desirable for the electrode-to-electrode distance of the closest planar electrodes. When the electrode-to-electrode distance is less than 10 μm, the electrodes are so close to one another that the probability for the cell bodies to adjoin via cell protrusions decreases. Furthermore, wiring of lead wires become difficult. When the electrode-to-electrode distance exceeds 1000 μm, lead wires can be easily wired but as it is rare for the cell protrusions of cultured nerve cell to elongate as far as about 1000 μm, the probability of the cell body to be located on the electrode decreases. Even under general conditions, about 200-300 μm is desirable for the electrode-to-electrode distance because the length of cell protrusions of a cultured cell is about 200-300 μm on average for central nervous system cells of mammals.

With respect to the electrode area, in order to avoid electrode breakage when electric stimulation is applied to the cell over a long time, it is necessary to reduce resistance at the interface with the culture medium, requiring a size exceeding a certain level. However, as the electrode area increases and the resistance at the interface with the culture medium reduces, the electric activity of the cell to be measured decreases and the signal to noise (S/N) ratio decreases. That is, if the current value I is constant, it follows from I = V/R that the potential V to be measured reduces with decreasing resistance R. That is, the electrical activities of the cell to be measured decrease and the S/N ratio lowers. Consequently, the electrode area must carefully be adjusted; it is desirable for the electrode area to be from 3×10^2 to 4×10^2 μm^2.

In order to bring the surface resistance of the electrode section down to 10 Ω/cm^2 or less, the ITO top surface is coated with metal. Examples of coating material include Ag, Al, Bi, Au, Cu, Cr, Pt and Co, but with low toxicity to nerve cells taken into account, the use of Au or Pt is desirable. The coating thickness is not, in particular, limited, but is about 50 nm and, in general, these materials are evaporated on the insulating substrate and are formed into desired patterns by etching using a photoresist.

By dripping a platinum salt solution on the electrode and electrolyzing it to deposit platinum black on the electrode, it is possible to coat the electrodes.

In addition, according to a preferred embodiment of the invention described previously, holes in the insulating layer of the planar electrode are formed to expose electrodes not only to give electrical stimulation to the cell body cultured on the planar electrode but also to detect electrical activities from adjoining cell bodies which are located at the central portion of the electrode.

Arranging lead wires stretched from the electrode nearly radially eliminates the capacitance between lead wires, reduces the time constant, and improves the measuring accuracy.

The configuration in which the electrode center portion of the planar electrode of the invention is located at each intersection of lattices of 8 × 8 or smaller enables the lead wire to be radially installed, and from the viewpoint of particularly forming as many electrodes as possible and providing and recording multi-point stimulation simultaneously, it is desirable to install electrodes at each intersection of the 8 × 8 lattices.

Now referring the following specific embodiments, the planar electrode of the invention will be described in further detail.

(Embodiment 1)

First, fabrication of a planar electrode wiring section is described. As the insulating substrate 3 of the planar electrode in Figs. 1 and 3, 50 × 50 × 1 mm hard glass ("IWAKI CODE 7740 GIASS" - Iwaki Glass Co., Ltd.) was used; this is a transparent insulating material with high mechanical

strength.

Referring to Fig. 3, for the material of electrode 1 and lead wire 2, ITO was used, and on the whole surface of the insulating substrate 3 of the hard glass, ITO was evaporated to form a layer about 100 nm thick, which was followed by rinsing.

Then, the substrate was exposed to light through a photoresist so that the central portion of each electrode 1 was located on each intersection of 8 × 8 lattices (position 5 as shown in Fig. 2), the center-to-center distances of nearest electrodes of each electrode were equal, and lead wire 2 formed the pattern of electrode 1 and lead wire 2 in which lead wire 2 was stretched radially. It was then etched with ITO in a solution which was made up using demineralized water, hydrochloric acid, and nitric acid in a volume ratio of 50:50:1, and the photoresist was removed. The wiring portion with electrode 1 being 60 μm in diameter, lead wire 2 being 30 μm wide, and a center-to-center distance of electrodes of 300 μm was thus formed.

Then, for insulating layer 4, negative photosensitive polyimide (hereinafter called "NIP") was spin-coated so that a film 1 μm thick was formed after drying, and an insulating layer pattern was exposure-formed so that a 50 μms square hole 5 was produced at the center of each electrode of the wiring section as shown in Fig. 2. Furthermore, to the exposed portion of each electrode (that is, the inside of the 50 μms square), gold 6 was evaporated in a film thickness of 50 nm.

The contact with the external circuit of the section near the end opposite to electrode 1 of lead wire 2 was coated with gold 7 and nickel 8 to improve durability.

In this embodiment, ITO was used for electrode 1 and lead wire 2, NPI for the insulating layer, and gold for the electrode surface coating material, but it has already been stated that the material used shall not be limited to these.

The process of producing the planar electrode of the invention is not limited to the method described in this embodiment.

(Embodiment 2)

Next, the culture of nerve cells on the planar electrode is described.

On the planar electrode formed in Embodiment 1, cerebral visual cortex cells of rats were cultured as the nerve cells.

Now, the culture method will be discussed in detail.

(a) Brains of fetuses of SD rats at 14-18 days of pregnancy were removed and immersed in iced Hanks' Balanced Salt Solution (hereinafter called "HBSS").

(b) From the brains in the iced HBSS, visual cortices were cut out and transferred to Eagle's minimum essential medium (hereinafter called "MEM") liquid.

(c) In the MEM liquid, the visual cortices were cut into as small pieces as possible, 0.2 mm square at maximum.

(d) The visual cortices cut into small pieces were placed in centrifugal tubes (test tubes for centrifugal separation), and after washing with HBSS free from calcium and magnesium (hereinafter called "CMF-HBSS") three times, they were dispersed in a suitable volume of the same liquid.

(e) In the centrifugal tubes of Step (d), a CMF-HBSS solution of trypsin (0.25 wt%) was added to double the total volume. With gentle stirring, enzymatic processes were allowed to take place while the solution was incubated at 37 °C for 15 to 20 minutes.

(f) DMEM/F-12 mixture medium in which Dulbecco modified Eagle's medium (DMEM) and HamF-12 medium were mixed in a volume ratio of 1:1 was added to the centrifugal tube subjected to Step (e) to further double the total volume. With a Pasteur pipette with a reduced diameter produced by fire-polishing the tip end with a burner, gently repeating pipetting (about 20 times at maximum), the cells were unravelled.

(g) Centrifugation was carried out for about 5 minutes at 9806.65 m/sec^2 (that is, 1000 g). Upon completion of centrifugation the supernatant was discarded and the precipitate was suspended in DMEM/F-12 mixture medium containing FCS 5%.

(h) Step (g) was repeated two more times (a total of 3 times).

(i) The precipitate finally obtained was suspended in the DMEM/F-12 mixture medium containing 5% FCS and using an erythrocytometer, the cell concentration in the suspension liquid was measured. Using the similar medium, the cell concentration was adjusted to be 1×10^6 to 5×10^6 cells/mL.

(j) In a well for cell culture formed by affixing a plastic cylinder 25 mm in diameter and 6 mm high to the planar electrode with the planar electrode center aligned with the plastic cylinder center, 500 μL of the DMEM/F-12 mixture medium containing 5% FCS was added in advance and heated in a CO_2 incubator (air content: 95 vol%; CO_2 content: 5 vol%; relative humidity: 97%; Temperature: 37 °C).

(k) In the well of Step (j), 100 μL of the suspension liquid with the cell concentration adjusted was gently added and again let stand in the CO_2 incubator.

(l) Three days after the performance of Step (k), one half the medium was replaced with a new one. For the replaced medium, the DMEM/F-12 mixture medium not containing FCS was used.

(m) Thereafter, half of the medium was replaced in the similar manner every 4 to 5 days.

Over the series of these operations, nerve cells of cerebral visual cortices of rats were cultured on the planar electrodes.

The cells grew successfully even on the insulating layer (NPI) and even on the electrodes with gold evaporated on them. Consequently, the use of the electrodes suitably located for the stimulation electrodes or recording electrodes enabled the simultaneous multi-point measurement of the electrical activities of nerve cells.

Figs. 4 and 5 show examples of electrical responses (potential changes) of nerve cells at the electrodes located at suitable places recorded before and after constant current stimulation of 100 μA was provided over one week at a frequency of 1 Hz via the electrodes suitably located in the planar electrode of the invention. Fig. 4 shows the electrical responses of the nerve cells before stimulation, while Fig. 5 shows the electrical responses of the nerve cells after stimulation.

In addition, Figs. 6 and 7 show examples of electrical responses of nerve cells recorded before and after long-term stimulation was applied under the same conditions as above, using a planar electrode whose surface is not coated with gold. Fig. 6 shows the records of electrical response of nerve cells before stimulation, while Fig. 7 shows the records of electrical response of nerve cells after stimulation.

In Figs. 4 through 7, the arrow marks show the artifacts generated as a result of application of stimulation current and the arrow head shows a potential change generated by electrical activities of nerve cells.

As is clear from Fig. 6, when the planar electrode whose surface is not coated with gold is used, generation of artifacts is great, while when the planar electrode of one embodiment of the invention shown in Fig. 4 is used, generation of artifacts is suppressed.

As is clear from Fig. 7, when the planar electrode surface is not coated with gold, generation of artifacts is greater after than before stimulation; the electrical activities of the nerve cells are hidden by the artifacts and measurement is disabled. In contrast, when the planar electrode of one embodiment of the invention as shown in Fig. 5 is used, same as in the case shown in Fig. 4, generation of artifacts is suppressed and the electrical activities of the nerve cells are successfully recorded.

There are many other methods than those described above for the culture of nerve cells on the planar electrode of the invention.

The invention may be embodied in other specific forms without departing from the spirit or essential characteristics thereof. The disclosed embodiments are to be considered in all respects as illustrative and not restrictive, the scope of the invention being indicated by the appended claims rather than by the foregoing description and all changes which come within the meaning and range of equivalency of the claims are intended to be embraced therein.

Claims

1. A planar electrode comprising an insulating substrate, a multiplicity of electrodes on said substrate with an equal distance between adjacent electrodes, a wiring section in which lead wires are installed nearly radially from said electrodes, and an insulating layer covering said lead wires, said electrodes each having an area from 3×10^2 to 4×10^2 μm^2.

2. The planar electrode according to claim 1 wherein the distance between adjacent electrodes is from 10 to 1000 μm.

3. The planar electrode according to claim 1 or 2, wherein the insulating layer covering the lead wires has holes over each electrode and is provided over substantially the entire surface of said insulating substrate except in the vicinity of contacts between an external circuit and the lead wires.

4. The planar electrode according to claim 1 or 2, wherein the insulating substrate comprises a transparent material.

5. The planar electrode according to claim 1 or 2, wherein the electrodes and the lead wires are made of a transparent material.

6. The planar electrode according to claim 1 or 2, wherein the electrodes and the lead wires each are made from indium tin oxide, tin oxide, Cr, Au, Cu, Ni, or Al.

7. The planar electrode according to claim 1 or 2, wherein said insulating layer comprises a transparent material.

8. The planar electrode according to claim 1 or 2, wherein said insulating layer is made from polyimide resin, negative photosensitive polyimide resin, epoxy resin, acrylate resin, polyester resin, or polyamide resin.

9. The planar electrode according to claim 1 or 2, wherein the surface resistance of said electrode is 10 Ω/cm^2 or lower.

10. The planar electrode according to claim 1 or 2, wherein surfaces of said electrodes are covered with platinum, platinum black, or gold.

11. The planar electrode according to claim 1 or 2, wherein centers of the electrodes are located at each intersection of an 8 × 8 lattice.

12. The planar electrode according to claim 3, wherein one or more of the insulating substrate, the electrodes, the lead wires and the insulating layer is made of a transparent material.

13. The planar electrode according to claim 12, wherein one or both of the electrodes and the lead wires is made from indium tin oxide, tin oxide, Cr, Au, Cu, Ni, or Al.

14. The planar electrode according to claim 12, wherein the insulating layer is made from polyimide resin, negative photosensitive polyimide resin, epoxy resin, acrylate resin, polyester resin or polyamide resin.

15. The planar electrode according to claim 3, wherein surfaces of said electrodes are covered with platinum, platinum black or gold.

16. The planar electrode according to claim 3, wherein centers of the electrodes are located at each intersection of an 8 × 8 lattice.

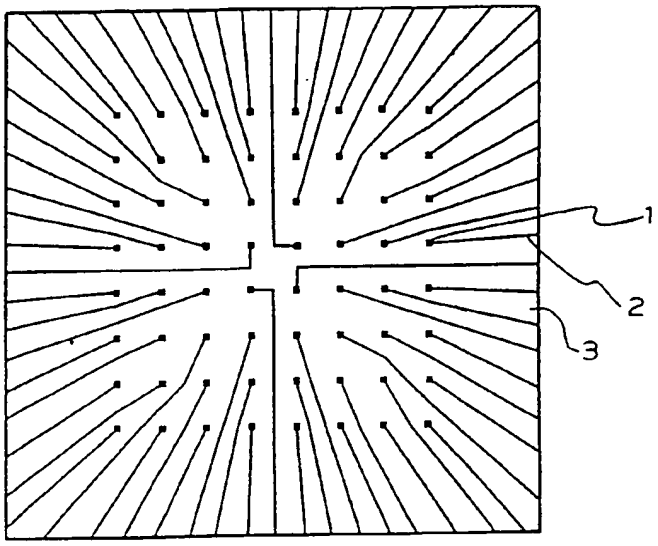

FIG.1

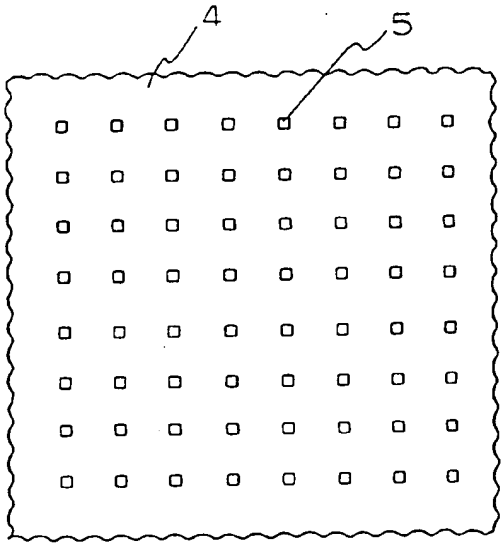

FIG.2

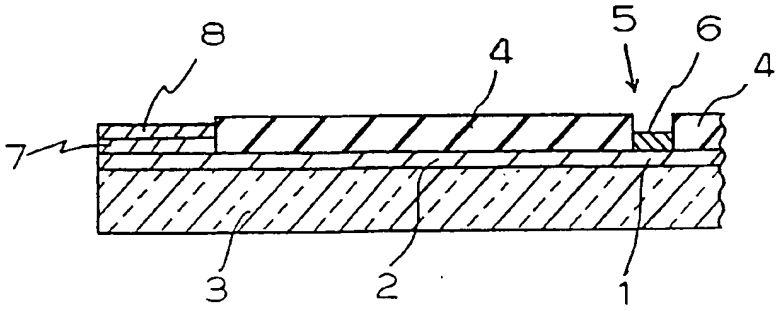

FIG.3

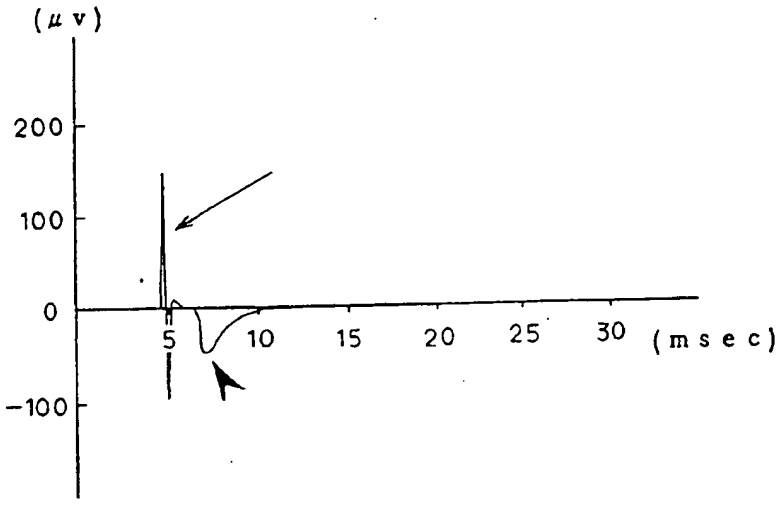
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FIG.4

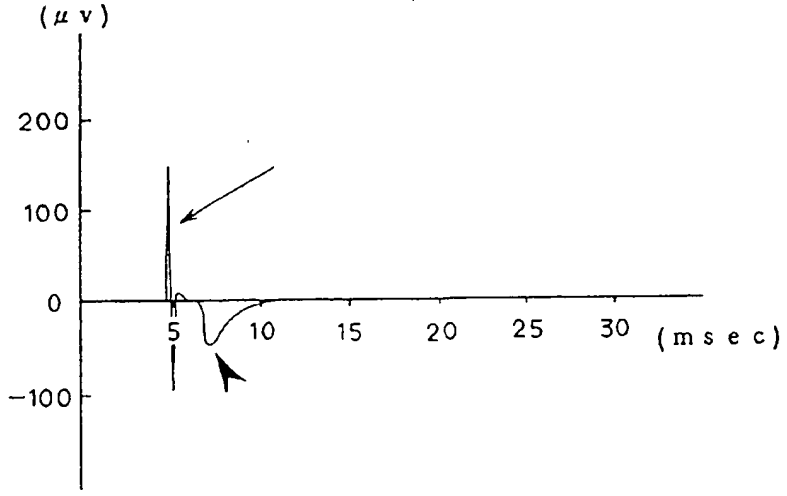
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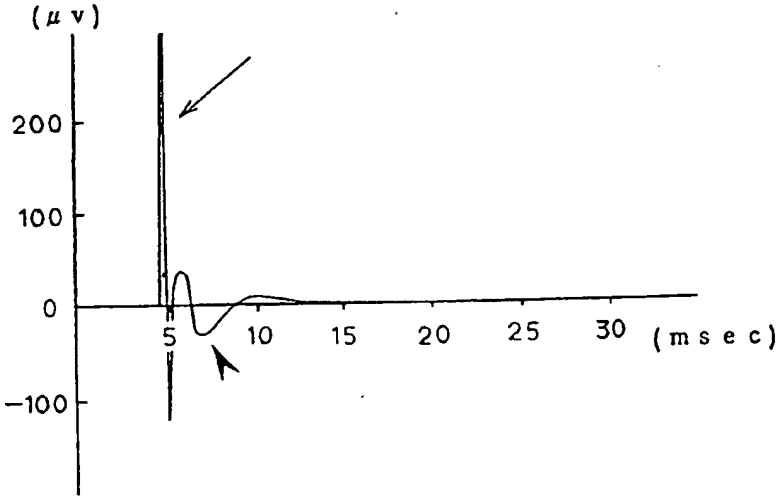
FIG.5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(msec)

FIG.6

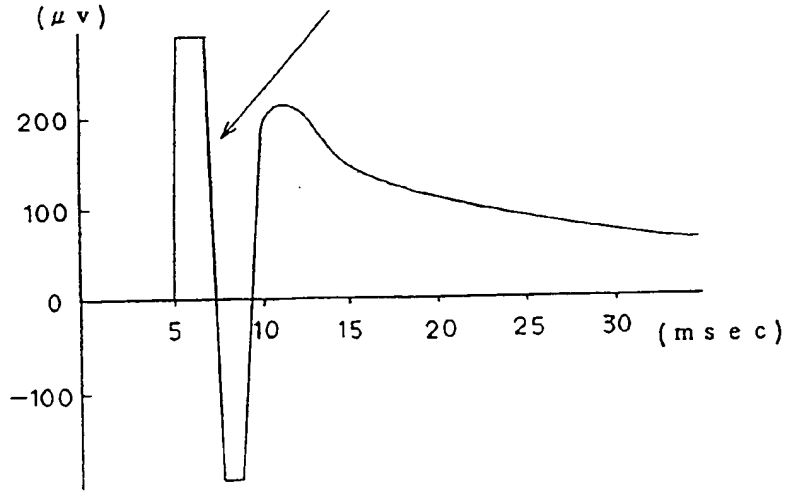
(μv)
200
100
0
−100
5
10
15
20
25
30
(msec)

FIG.7